**REMARKS**

Appreciation is hereby expressed to Examiner Dr. Grun for the interview so courteously granted on November 9, 2001. Pursuant to that interview, Claim 4 has been canceled and Claims 1, 3 and 11 amended to more definitely set forth the invention and obviate the rejection. At the outset, it is noted that Claims 1 and 3 have been amended to change "comprising" to "consisting essentially of" to more clearly distinguish from the prior art of record. The support for this amendment can be found in the Specification, page 10, lines 20-22, page 12, lines 4-8, 18-25, and page 20, lines 12-19, and page 10, lines 9-19, and Claim 11 has been amended to delete the term "the" to overcome the rejection under 35 U.S.C. § 112, second paragraph. The present amendment is deemed not to introduce new matter. Claims 1-6 and 9-16 are in the application.

Reconsideration is respectfully requested of the rejection of Claims 1-2, 5-6, 9-11 and 13 under 35 U.S.C. § 112, first paragraph.

In an effort to clarify the issues in this case, there is enclosed a schematic drawing which shows the mechanism of the measurement recited in Claim 1. This schematic drawing illustrates two cases, one in which a small amount of antigen is contained in a sample and a second case where a large amount of antigen is contained in a sample. In the first case shown on the schematic, little or no change in the absorbance occurs when the amount of antigen is small. The reason is that the insoluble carrier

aggregates to a low extent and thus the enzyme coupled to the insoluble carrier is inactivated by the enzyme inhibitor.

In the second case where a large amount of antigen is contained in the sample, change in absorbance occurs since the insoluble carrier aggregates to a large extent. In the second case, the enzyme couples to the insoluble carrier and is not inactivated by the enzyme inhibitor.

It is believed that principles of the inventions as recited in Claim 1 are clear from this explanation. In addition, it is believed that the principle of the invention called for in Claim 3 is clear by reference to the schematic showing the principles of measurements of Claim 3 which was included in the previous amendment filed on May 24, 2001. A copy of this schematic showing the operation of the procedure of Claim 3 is attached hereto for the convenience of the Examiner. In that method, the change in absorbance or signal is not based on the function of the enzyme inhibitor per se, but the same is due to the reaction between the substrate and the enzyme which is not inactivated by enzyme inhibitor.

With reference to the language "plural different combination" in Claims 6 and 13, the plural kinds of the antibody or antigen to different substances to be detected are coupled to not the same carrier, but different carriers, respectively. For example, in case of the measured substances being A and B, the reagent components consisting of a(A), b(A) and c(A) and the reagent

components consisting of a(B), b(B) and c(B) are separately prepared and then they are mixed. The antibody or antigen corresponding to A and the antibody or antigen corresponding to B are, therefore, not coupled to the same carrier but different carriers. Accordingly, if substrates being different in absorbing wave length to each other are used as the components c(A) and c(B), the substances A and B can be measured.

In view of this explanation, it is respectfully submitted that the rejection is unwarranted and the Examiner would be justified in no longer maintaining this rejection.

Reconsideration is respectfully requested of the rejection of Claims 2, 4, 11 and 16 under 35 U.S.C. § 112, second paragraph, as being indefinite. With respect to the rejection of Claim 2, it is respectfully submitted that Claim 2 clearly defines subject matter which adds a limitation to the invention recited in Claim 1. Particularly, in Claim 2, the first reagent comprises the component a, while the second reagent comprises the component b and c. This is believed to add a limitation which is not present in Claim 1 and, therefore, it is believed to be a proper dependent claim. With respect to the expression "the absorbance", Claim 11 has been amended to delete the reference to "the" and it is therefore believed that the rejection thereof is moot.

With respect to the method set forth in Claim 16, the component a provides a change in absorbance due to the aggregation while the components b and c provide a change in absorbance due to

coloring of enzyme. This can be seen in the principles of measurement of Claim 1 attached hereto.

In view of the foregoing, it is respectfully submitted that the amendments and explanations provided above render the rejection moot. Withdrawal of the rejection is accordingly respectfully requested.

Reconsideration is respectfully requested of the rejection of Claims 1-6 and 12-13 under 35 U.S.C. § 102(b) as being anticipated by Kasahara '792.

In Kasahara '792, there are competitive reactions between antigen to be measured, antigen coupled to the solid carrier, enzyme inhibitor coupled to a solid carrier, and combination material coupling antibody to the antigen and the enzyme. The method of Kasahara '792 utilizes coloring due to enzyme raction. Therefore, the cited prior art differs in principle from the present invention wherein not only the coloring due to the enzyme reaction but also due to the aggregation of the insoluble carriers is utilized.

In the present invention, the carriers are used not only to immobilize the antibody, enzyme or the like, but only to be aggregated by the antigen-antibody reaction. In contrast, the carrier in Kasahara '792 is used only to immobilize the antigen, enzyme and the like. For example, Kasahara '792 describes on column 4, line 67, the carrier or spherical beads having a diameter of 6 mm. Such spherical beads cannot be aggregated. Independent

Claims 1 and 3 have been amended to make clear that the insoluble carrier is capable of aggregation. This feature is believed to distinguish from the carrier of Kasahara '792

As described in the foregoing, it is quite clear that the present invention differs from Kasahara '792.

In addition, in the final rejection the Examiner concludes that in Kasahara '792 the antigen (or antibody) and the enzyme (or enzyme inhibitor) are coupled to the solid phase, and that Kasahara '792 and the present invention are the same in composition.

In Kasahara '792, however, the same substance as substance to be measured has to be coupled to the solid phase. For example, if the antigen is measured, an antigen must be coupled to the solid phase, since competitive reactions are utilized.

By contrast, in the present invention, the antibody is coupled to the insoluble carrier, when the antigen is measured. Accordingly, in the present invention, the substance immunologically reactive to the substance to be measured is coupled to the carrier. This feature is also now set forth in amended Claims 1 and 3 herein.

Reconsideration is respectfully requested of the rejection of Claims 1-6 and 12 and 13 under 35 U.S.C. § 102(b) as anticipated by Kasahara, et al. '105 for reasons of record.

As to Kasahara '105, this prior art utilizes the principle of Kasahara '792 as well as abizine-biotine system and thus the same merely shows the method and reagent which are more different from

the present invention than Kasahara '792, as described above.

In view of the foregoing, it is respectfully submitted that the rejection fails in view of the difference in principle and methods and reagents used in the Kasahara '105 reference and the present invention. Consequently, the Examiner would be justified in no longer maintaining the rejection. Withdrawal of the rejection is accordingly respectfully requested.

Reconsideration is respectfully requested of the rejection of Claims 1-6, 9, 10, and 12-15 under 35 U.S.C. § 103(a) as being unpatentable over Kasahara, et al. '792 or Kasahara, et al. '105 in view of Ashihara '048 for reasons of record.

The Ashihara '048 reference has been discussed at length in previous amendments. However, it should be noted here that the Ashihara '048 reference describes that the enzyme inhibitor and the anti-enzyme antibody are used. However, Ashihara '048 does not use an insoluble carrier, and thus the reagent and method of Ashihara are entirely different from the present invention.

In view of the foregoing, it is respectfully submitted that the Kasahara '792 and '105 are completely different in principle and operation from the present invention, and thus even if Kasahara '792 and '105 and the teachings of Ashihara '048 are combined, they do not individually or in combination yield the process of the present invention or the reagents used therein.

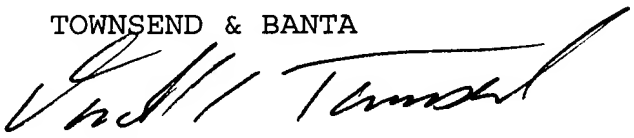
It is therefore respectfully submitted that the rejections fail and that the process of the present invention clearly

patentably distinguishes from the references of record. Consequently, the Examiner would be justified in no longer maintaining this rejection. Withdrawal of the rejection is accordingly respectfully requested.

In view of the foregoing, it is respectfully submitted that the application is now in condition for allowance and early action and allowance thereof is accordingly respectfully requested. If there is any reason why the application cannot be allowed at the present time, it is respectfully requested that the Examiner contact the undersigned at the number listed below to resolve any problems.

Respectfully submitted

TOWNSEND & BANTA



Donald E. Townsend
Reg. No. 22,069

TOWNSEND & BANTA
1225 Eye Street, N.W.
Suite 500, #50028
Washington, D.C. 20005
(202) 682-4727

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**MARKED-UP VERSION OF AMENDED CLAIMS 1, 3 AND 11**

1. (Thrice Amended) An immunoassay reagent for use in a quantitative determination of a target antigen or antibody present in a sample, said reagent [comprising] consisting essentially of the following components:

(a) An insoluble carrier which carries and is coupled to an enzyme and an antibody or antigen reactive with said target antigen or antibody, said insoluble carrier comprising at least one selected from the group consisting of an organic polymer powder article, microorganism, blood cell and cell membrane fragment, said insoluble carrier being capable of aggregation;

(b) an enzyme inhibitor for inhibiting activity of said enzyme; said enzyme inhibitor being in a free state uncoupled to an antigen or antibody and

(c) a substrate with which the enzyme reacts, said components (a)-(c) being maintained separate and apart and mixed together only with a sample containing the target antigen or antibody.

3. (Thrice Amended) An immunoassay reagent for use in quantitative determination of a target antigen or antibody present in a sample, said reagent [comprising] consisting essentially of the following components:

(a) an insoluble carrier which carries and is coupled to an enzyme inhibitor and an antibody or antigen reactive with said

target antigen or antibody, said insoluble carrier comprising at least one selected from the group consisting of an organic polymer powder particle, microorganism, blood cell and cell membrane fragment, said insoluble carrier being capable of aggregation;

(b) an enzyme whose activity is inhibited by said enzyme inhibitor; said enzyme being in a free state uncoupled to an antigen or antibody and

(c) a substrate with which the enzyme reacts, said components (a)-(c) being maintained separate and apart and sequentially mixed together only with a sample of target antigen or antibody.

11. (Thrice Amended) An immunoassay method for quantitatively determining a target antigen or antibody present in a sample, comprising:

mixing the immunoassay reagent of claim 1 with the sample to thereby facilitate an enzyme reaction and an antigen-antibody reaction resulting in agglutination of the insoluble carrier; and

measuring [the] absorbance of the resulting mixture as an index of an amount of target antigen or antibody in the sample.